

**UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION**

IN RE: NATIONAL PRESCRIPTION)	MDL 2804
OPIATE LITIGATION)	
)	Case No. 1:17-MD-2804
THIS DOCUMENT RELATES TO:)	
)	Judge Dan Aaron Polster
<i>Track Three Cases</i>)	
)	<u>OPINION AND ORDER REGARDING</u>
)	<u>THE EXPERT OPINIONS OF</u>
)	<u>DR. KATHERINE KEYES</u>

The Pharmacy Defendants move to exclude certain opinions and testimony of Dr. Katherine Keyes. Doc. #: 3858. Plaintiffs filed a response in opposition and Defendants filed a reply in support. Upon careful review of the parties' briefs and supporting documents, including the expert report of Dr. Keyes, for the reasons stated below, Defendants' Motion is **DENIED**.

Legal Standard

The Court hereby incorporates the legal standard set forth in the Court's Opinion and Order regarding *Track One-A* Defendants' motion to exclude the opinion and testimony of Prof. Meredith Rosenthal. *In re Nat'l Prescription Opiate Litig.*, No. 1:17-MD-2804, 2019 WL 3934597, at *1–*5 (N.D. Ohio Aug. 20, 2019) (Doc. #: 2495 at 1–10).

Analysis

Dr. Katherine Keyes is an Associate Professor of Epidemiology at Columbia University where she received tenure in 2020. She specializes in substance use and substance use disorders epidemiology. She is a highly cited author, having published 300 peer-reviewed articles, editorials, and book chapters, as well as two textbooks on epidemiological methods: *Epidemiology Matters: A New Introduction to Methodological Foundations*; and *Population Health Science*, both published by

Oxford University Press. Her textbooks instruct on the theoretical and methodological foundations of the science of public health.

Dr. Keyes’ expertise on opioid-related harm includes “large scale survey data and vital statistics analyses, as well as the development of theories, hypotheses, and publishing findings concerning the role of macro-social factors in producing opioid epidemics.” Keyes Rpt. at 2. She is also “an investigator on the HEALing Communities Study, a large, \$350 million dollar NIH-funded initiative aiming to reduce opioid overdose by 40 percent in four states, including New York, Ohio, Kentucky, and Massachusetts.” *Id.* Her report indicates that she has “published 28 peer-reviewed journal articles on opioid use and related harms (and many more on drug use disorders more generally),” which, the Court notes, is 9 more than she had published at the time of her *Track One* Report in March of 2019. *Id.*

The Pharmacy Defendants seek to exclude three portions of Dr. Keyes’ opinions. First, they “seek to exclude Dr. Keyes’ marketing testimony and opinions as to Defendants.” Motion at 1. Second, the Pharmacy Defendants seek to exclude Dr. Keyes’ opinions regarding the causal link between prescription opioid use and synthetic opioid harms. Finally, they ask that, if the Court refuses to exclude her causation opinions outright, it instead issue a limiting instruction explaining that Dr. Keyes’ “definition [of causation] differs from legal causation.” *Id.* at 2. The Court addresses each of these requests in turn.

Marketing Causation Opinion

The Pharmacy Defendants first ask the Court to exclude Dr. Keyes’ marketing causation opinion, specifically as it relates to the Pharmacy Defendants, “[1] for the reasons it did so previously and for additional reasons specific to Defendants here—namely, that [(2)] Dr. Keyes’ methodology is flawed as to Defendants, and [(3)] any such opinions would be misleading, confusing, and unfairly prejudicial.” Motion at 1. The Pharmacy Defendants’ methodology and

prejudice arguments were before the Court in Track One, but because the Court concluded Dr. Keyes was not qualified to offer her marketing opinions, it did not address those arguments at that time. *See In re Nat'l Prescription Opiate Litig.*, No. 1:17-MD-2804, 2019 WL 4054998, at *10, n.13 (N.D. Ohio Aug. 28, 2019) (Doc. #: 2549 at 21, n.13) (“In light of this ruling, the Court does not address Defendants’ arguments that Keyes’ opinions on marketing causation are unreliable and unfairly prejudicial.”). Because the Court now declines to exclude any of Dr. Keyes’ marketing causation opinions, each rationale asserted by the Pharmacy Defendants is addressed fully below.

1. The Court’s Prior Reasoning in *Track One*

In *Track One*, the Court declined to allow Dr. Keyes to testify regarding one very narrow and specific marketing causation opinion. That was “the opinion contained in the first full paragraph on page 22 of her [*Track One*] Report, in which she finds that Defendants’ marketing efforts caused an increase in the supply of prescription opioids.” *Id.* at *10 (Doc. #: 2549 at 21). The reasons the Court gave for not permitting Dr. Keyes to offer this single opinion were threefold. **First**, in her *Track One* Report, the Court was concerned that Dr. Keyes only cited “to one study that demonstrated a statistically significant connection between payments to physicians and increases in opioid-related overdoses.” *Id.* at *9 (Doc. #: 2549 at 20). **Second**, the Court did not believe Dr. Keyes had “shown that she applied epidemiological methods to determine that a cause-effect relationship may be inferred from the study that she cites.” *Id.* **Third**, the Court concluded Plaintiffs had not “shown that [Dr. Keyes’ epidemiological] expertise include[d] determining the effect of pharmaceutical marketing on doctors’ prescribing practices.” *Id.* at *10 (Doc. #: 2549 at 21).

In their current briefing, Plaintiffs now address each of these concerns. Specifically, in response to the Court’s first two criticisms, Plaintiffs assert Dr. Keyes “reviewed numerous peer-reviewed studies, not just one,” Response at 5; *see also id.* at 5, n.4 (listing additionally reviewed

sources), and explain Dr. Keyes also more carefully and thoroughly explained the epidemiologic methodology she used to support her finding of causality (i.e., application the Bradford Hill criteria).¹ *See id.* (citing Keyes Rpt. at 33). In response to the Court’s third concern, Plaintiffs assert that, in reaching its conclusion in *Track One*, “the Court did not have before it evidence that Dr. Keyes is an investigator in a study analyzing, among other things, the effect of detailing (face-to-face meetings with physicians, either by pharmaceutical representatives as part of their marketing efforts, or by academic or public health physicians in an effort to combat the effects of drug-company marketing) on opioid prescribing habits.”² *Id.* at 4. This additional experience, Plaintiffs assert, shows that Dr. Keyes is “qualified through ‘knowledge, skill, **experience**, training, or education’ to offer opinions regarding pharmaceutical marketing causation.” *In re Opiate*, 2019 WL 4054998, at *10 (Doc. #: 2549 at 21) (citing Fed. R. Evid. 702) (emphasis added).

In their Reply, the Pharmacy Defendants argue none of this demonstrates a change in Dr. Keyes’ qualifications. Reply at 5. They assert that, even though Dr. Keyes’ additional experience was not before this Court in *Track One*, it was before Judge Faber in *Track Two* and Judge Faber also excluded her marketing opinions in his bench trial.³ The Pharmacy Defendants then assert she did not cite the work she did for the NIH study as supporting her opinions, nor did she talk to any doctors *in*

¹ “The factors that guide epidemiologists in making judgments about causation . . . reflect criteria proposed by the U.S. Surgeon General in 1964 in assessing the relationship between smoking and lung cancer and expanded upon by Sir Austin Bradford Hill in 1965 and are often referred to as the Hill criteria or Hill factors.” Reference Manual on Scientific Evidence, Reference Guide on Epidemiology at 599–600 (Fed. Judicial Ctr. 3d ed. 2011) (hereafter “FJC Reference Manual”).

² The study, referred to here by Plaintiffs, is the National Institute of Health (“NIH”) funded HEALing Communities Study. *See* Keyes Rpt. at 2.

³ Plaintiffs respond that Judge Faber’s order excluding the marketing causation opinion of Dr. Keyes is not precedential, because it was issued without opinion. As a notable counter-point to the Pharmacy Defendants position, Judge Garguilo, in the NY State litigation, did **not** exclude any of Dr. Keyes’ opinions. Defendants state this also is not precedential because “that decision did not list marketing causation as an issue raised by the defendants and did not address those arguments.” Motion at 5, n.5. But her marketing causation opinions were in her New York report. The Court concludes that neither Judge Faber’s nor Judge Garuilo’s order carries much precedential value here, given they simply do not address the question at issue on the merits.

*Lake or Trumbull Counties.*⁴ *Id.* But the Pharmacy Defendants do not contradict Plaintiffs' representations that Dr. Keyes has obtained additional, specific experience since *Track One*, and do not deny she has explained more fully her causation methodology; nor do they squarely address the value of her experience.

The Court concludes that Dr. Keyes' expertise in epidemiology, in light of her review of additional, relevant documents and studies and the time she has spent investigating the effects of pharmaceutical detailing, qualifies Dr. Keyes to draw conclusions about the causal-relationship between pharmaceutical marketing and the increased supply of prescription opioids. This conclusion, now well-supported by Dr. Keyes' relevant experience, easily falls within the purview of her epidemiologic expertise. At its core, the science of epidemiology examines association, correlation, and causation between population-level public health events, which frequently include macro-social factors such as politics, culture, or economics. Further, Dr. Keyes' opioid-specific experience includes analyses of various "macro-social factors in producing opioid epidemics." Keyes Rpt. at 2. As an accomplished epidemiologist, Dr. Keyes is well-situated to draw informed causation opinions using the Bradford Hill criteria. As an epidemiologist with experience investigating pharmaceutical industry detailing in particular, the Court is now convinced she does have the requisite experience to form an opinion on the (frankly, unremarkable) idea that increases in effort and funding spent on marketing opioids to doctors worked to increase the number of opioids prescribed. Such an epidemiological conclusion does not require special knowledge of any particular defendants' marketing materials, nor does it require both a PhD in the economics of

⁴ These two arguments are not well-taken. Dr. Keyes does refer to her experience as an investigator in the HEALing Communities Study in her Background and Qualifications section. *See* Keyes Rpt. at 2. She also states, broadly, that she is "well-qualified to review the literature and offer opinions based on the evidence *and [her] own experience.*" *Id.* (emphasis added). As discussed in greater detail, *infra*, the fact she did not talk to specific doctors in Lake or Trumbull County is not germane to her opinions as an epidemiologist.

opioid marketing and an LLM on the regulatory schemes governing opioid marketing. Accordingly, Dr. Keyes will be allowed to testify regarding her marketing causation opinion.⁵

2. Dr. Keyes' Methodology with Respect to Pharmacy Defendants

The Pharmacy Defendants next assert that Dr. Keyes' methodology is flawed with respect to them, in particular. In making this argument, it appears the Pharmacy Defendants miscomprehend two fundamental concepts. First, the Pharmacy Defendants implicitly assume that Dr. Keyes, in her own testimony and by herself, must prove one or more of them caused the opioid crisis. This Court has explained, in *Track One*, that Plaintiffs do not have to prove their entire case through one expert. *See In re Nat'l Prescription Opiate Litig.*, No. 1:17-MD-2804, 2019 WL 4043938, at *4 (N.D. Ohio Aug. 26, 2019) (Doc. #: 2519 at 7) ("Plaintiffs are entitled to utilize different experts to support different portions of their case."); *see also United States ex rel. Landis v. Tailwind Sports Corp.*, No. 10-CV-00976, 2017 WL 5905509, at *6 (D.D.C. Nov. 28, 2017). It is true, of course, that to prevail at trial, Plaintiffs must show the conduct of each Defendant individually was a substantial factor in creating a public nuisance. However, it is not true that, just because *Dr. Keyes* does not link a specific Defendant to a specific type of conduct in her report, her testimony must be excluded. Plaintiffs may cite other evidence, or rely on the testimony of other experts, to make those connections. That Dr. Keyes does not refer, specifically, to any particular Defendant's marketing materials in her report does not make it unreliable.

The Pharmacy Defendants' second misconception is that an epidemiologist's methodology is flawed if she does not consider elements of specific causation. *See Motion at 10* ("This case is about whether conduct by *specific* Defendants caused a public nuisance in *specific* counties. Dr. Keyes'

⁵ The Court notes that, although it now allows—in light of new evidence not previously before it—Dr. Keyes to opine on marketing causation generally, as discussed further below, the burden remains on Plaintiffs to prove that the Pharmacy Defendants *in this case* participated in the pharmaceutical opioid marketing conduct described in the studies cited and relied upon by Dr. Keyes. Without evidence of such conduct, the relevance of Dr. Keyes' marketing causation opinions is greatly diminished, and the Court will be receptive to the Pharmacy Defendants' live objections.

opinions, however, do not evaluate any *specific* Defendant's conduct, let alone any such conduct by a *specific* Defendant in Lake or Trumbull Counties.") (emphasis added). The primary focus of the science of epidemiology is not on specific causation, but on general causation. *See* FJC Reference Manual at 552 ("Epidemiology focuses on the question of general causation (i.e., is the agent capable of causing disease?) rather than that of specific causation (i.e., did it cause disease in a particular individual?)). Put another way, the subject of Dr. Keyes' report is about whether and to what extent the various factors she identifies are "capable of causing disease" (in this case, opioid use disorder and addiction at epidemic levels). To do this, Dr. Keyes has evaluated data from peer-reviewed epidemiological studies to determine, first, whether there is an association between two population-level events. In the case of Dr. Keyes' marketing opinion, those events are "increased pharmaceutical industry marketing" and "increased supply of prescription opioids." Because Dr. Keyes found an association between those events, following standard epidemiological methodology, her report explains she took the next step and evaluated the Bradford Hill criteria to make a scientific judgment regarding whether the relationship between the associated events is causal. Dr. Keyes concluded, in her expert opinion, it was. *See* Keyes Rpt. at 33–34.

There is nothing methodologically unsound about Dr. Keyes' report simply because she did not tie the specific conduct of any particular Pharmacy Defendant to that described in her marketing opinion. That is Plaintiffs' burden. Plaintiffs must prove the Pharmacy Defendants participated in the pharmaceutical industry marketing described by Dr. Keyes as increasing the supply of prescription opioids, and that the increased supply of prescription opioids in Plaintiffs' Counties caused the nuisance there. That Dr. Keyes does not offer that specific opinion does not make her testimony unreliable.

3. Unfair Prejudice

Finally, the Pharmacy Defendants assert that, if the Court allows a jury to hear that pharmaceutical opioid marketing by the “pharmaceutical opioid industry” caused an increase in pharmaceutical opioid sales and supply, they would be unfairly prejudiced. The Pharmacy Defendants assert that “Dr. Keyes cites studies that relate solely to marketing by manufacturers to physicians, not ‘marketing generally.’” Reply at 3. This issue is slightly different than the one addressed below regarding causation more broadly. Here, the Pharmacy Defendants are concerned they will be unfairly and prejudicially “lumped in”⁶ with other pharmaceutical industry members—particularly, opioid manufacturers—if Dr. Keyes is allowed to testify that “pharmaceutical opioid marketing,” generally, caused an increase in opioid supply. Their concern is unfounded because they can easily cure any potential prejudice.

As evidence of the potentially confusing effect of a “pharmaceutical opioid industry” generalization, the Pharmacy Defendants highlight one of the studies Dr. Keyes relied on in her report: *Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing*. The study was described, by its own authors, as “stud[ying] the extent to which **pharmaceutical industry marketing** of opioid products to physicians during 2014 was associated with opioid prescribing during 2015.” Hadland SE, et al, *Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians With Subsequent Opioid*

⁶ In a prior ruling on a related issue, where Defendants sought to forbid Plaintiffs from referring to “Defendants” collectively, the Court acknowledged it could be “confusing and unfair for Plaintiffs to lump all of the Defendants together;” but the Court “decline[d] to make a blanket ruling on this issue,” instructing instead that, “when the attorneys and witnesses use the term ‘Defendants,’ if they are not referring to all of the Defendants in the case, they must be specific as to which Defendants they mean.” Evidentiary Order, Doc. #: 3058 at 63-4. This same rule will apply in *Track Three*, and the principle underlying this prior ruling is the same as the one reiterated here. Plaintiffs must prove their nuisance claims against each individual Pharmacy Defendant. Dr. Keyes is an epidemiologist. She may opine that opioid marketing, in general, led to an increase in opioid supply. To the extent Plaintiffs assert marketing by any *Track Three* Defendant caused a public nuisance, it remains Plaintiffs’ burden to prove that each specific Defendant participated in opioid marketing.

Prescribing, JAMA Intern. Med., Vol. 178, Issue 6, 861–63 (2018) (Motion Ex. 13) (emphasis added). The study identifies the specific marketing conduct analyzed. *See Id.* at 862 (“Marketing included speaking fees and/or honoraria, meals, travel, consulting fees, and education.”) (parentheticals omitted). The Court understands that the “pharmaceutical industry” is not on trial. This trial is about the conduct of these four Pharmacy Defendants. Thus, the specific conduct cited by this study and attributed to the “pharmaceutical industry” may not be attributable to any of these four Pharmacy Defendants. But the study still stands for the proposition that marketing of opioids is associated with an increase in opioid dispensing, and the Pharmacy Defendants *did* market opioids.

The Pharmacy Defendants are free to point out on cross-examination that they did not engage in the type of marketing examined in the study, and to ask for an instruction from the Court reminding the jury that they are liable only for their own conduct and not that of any other members of the “pharmaceutical industry.” The Court is confident that the jury will understand this concept. In the end, that Dr. Keyes relied on studies and datasets that analyzed conduct of the pharmaceutical industry broadly, in which these Defendants assert they did not directly participate, goes to the weight of her opinion, not its admissibility.

Causation Opinions Relating Prescription Opioid Use to Synthetic Opioid Harms

Defendants further argue Dr. Keyes applies unreliable methodology to conclude prescription opioid use resulted in harms from illicit synthetic opioid use. Motion at 12–16. They challenge the opinion as lacking the necessary considerations of confounding facts, alternative explanations, and statistical association analysis. *Id.* at 12.

These arguments resurrect issues raised and ruled upon in the CTI Order denying Defendants’ Motion to exclude testimony concerning the “Gateway Hypothesis” advanced by Plaintiffs’ experts Katherine Keyes, Anna Lembky, and Jonathan Gruber. *In re Prescription Opiate Litig.*, 2019 WL 4043943 (N.D. Ohio Aug. 26, 2019) (Doc. #: 2518). There, the *Track One*

Defendants asserted “there is no scientific evidence that even purports to look at – let alone find a causal link between – properly prescribed pain patients and today’s heroin and fentanyl problems.” *Id.*, at *2 (Doc. #: 2518 at 4) (quoting Doc. #: 1858-1 at 6). Their motion contended none of the studies relied upon by the experts supported the experts’ “extreme position: that prescription opioid use has *caused* illicit heroin and fentanyl abuse today.” (Doc. #: 2515 at 1 (emphasis in original)). The Court rejected Defendants’ argument that the experts’ causation analysis failed to provide a sufficiently reliable foundation upon which to opine that prescription opiate use causes illicit opioid abuse. *In re Opiate*, 2019 WL 4043943, at *5–*6 (Doc. #: 2518 at 10–13). The Court noted that, to support their causal relationship opinions, Dr. Keyes and the other experts relied on studies concluding a high percentage of people used prescription opioids prior to using heroin, and on statistical data indicating strength of association, dose-response relationship, and a temporal relationship. *Id.*, at *5 (Doc. #: 2518 at 10–11). After examining the experts’ application of the Bradford Hill criteria to determine whether a correlation between variables indicates a causal relationship, the Court concluded that “the Experts’ opinions on causation are rooted in a reliable methodology sufficient to withstand *Daubert* scrutiny,” leaving the Defendants to “explain their critiques of the statistical methodologies the Experts rely on to the jury.” *Id.*, at *6 (Doc. #: 2518 at 11–13). The same outcome applies to the Pharmacy Defendants’ motion now before the Court, for the same reasons.

The Pharmacy Defendants’ present motion asserts survey data concerning percentages of people who first misuse prescription opioids before using heroin “reflects only a sequence of events and is not even a theoretical basis for inferring causation.” Motion at 13 & nn.14–16. Defendants cite studies identifying factors leading to use of heroin other than prior prescription opioid use, such as “common physiological, psychological, and sociological influences, [that] may

lead a person to heroin.” *Id.* Defendants offer a detailed critique of studies cited by Dr. Keyes and point out, for example: (1) a study finding research subjects typically used other drugs before prescription opioids and were multi-drug users; and (2) another study stating results should be “interpreted with caution in light of several limitations.” *Id.*

But Dr. Keyes’ full report dispels Pharmacy Defendants’ assertion that she failed to consider confounding factors or alternative explanations. Keyes Rpt. at 12–13 (discussing source selection and explaining the use of “randomized controlled trials” in order to mitigate any influence of confounding and bias). In any event, Pharmacy Defendants’ argument concerns the weight of her testimony, not its admissibility. *See Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 265 (4th Cir. 1999) (expert’s causation conclusion “should not be excluded because he or she has failed to rule out every possible alternative cause;” alternative causes suggested by a defendant “affect the weight that the jury should give the expert’s testimony and not the admissibility of that testimony”) (citing *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 156 (3d Cir. 1999)) (internal quotation marks omitted); *Dugger v. Union Carbide Corp.*, 2019 WL 4750568, at *5 (D. Md. Sept. 30, 2019) (where “epidemiological studies relied on by the plaintiffs’ experts fail to take into account certain confounding factors . . . challenges to the expert testimony . . . are more appropriately brought before a jury.”).

The Pharmacy Defendants also assert that none of the studies on which Dr. Keyes relies finds a causal relationship between opioids and heroin, nor do any studies find that 70–80% of heroin use is attributable to prescription opioid use. Motion at 14; Reply at 15. These assertions are belied by the record. Dr. Keyes’ report cites studies by Cicero, Lankenau, and Mateu-Gelabert in which data showed approximately 70–80% of individuals who used heroin in the last 20 years

started their opioid use with prescription opioids.⁷ Keyes Rpt. at 36. As Plaintiffs note, the Court previously concluded that the “trajectory – from addiction to prescription opioids to addiction to illicit opioids – finds support in the NASM report, the Lankenau and Cicero studies, and Keyes’ and Lembke’s first-hand clinical experience.” Response at 13 (citing *In re Opiate*, 2019 WL 4043943, at *5). Furthermore, Dr. Keyes’ methodology is now supplemented by recently published literature supporting her opinion,⁸ including a 2020 study finding each sequence of opioid use leads to an increase in heroin use.⁹ Keyes Rpt. at 28, 37–38.

The Pharmacy Defendants characterize Dr. Keyes’ reasoning as based on “the legally erroneous proposition that if heroin use is associated with prior use of prescription opioids, then so is any indirect consequence of heroin use;” and they argue that, as a legal question, it should be excluded. Motion at 15. Responding, Plaintiffs state, “Dr. Keyes does not offer opinions about *legal* causation. Rather, she is explaining the causal chain as a matter of fact.” Response at 16 (emphasis in original). The Court agrees with Plaintiffs. Defendants may argue their legal responsibility does not stretch so far as to include this causal chain, but the issue does not impact the reliability or admissibility of Dr. Keyes’ opinions.

⁷ See Keyes Rpt. at 34 & nn.162, 164, 176 (citing Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821–826. doi:10.1001/jamapsychiatry.2014.366; Mateu-Gelabert P, Guarino H, Jessell L, Teper A. Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. *J Subst Abuse Treat*. 2015;48(1):13–20. doi:10.1016/j.jsat.2014.07.002; Lankenau SE, Teti M, Silva K, Bloom JJ, Harocopos A, Treese M. Initiation into prescription opioid misuse among young injection drug users. *Int J Drug Policy*. 2012;23(1):37–44. doi:10.1016/j.drugpo.2011.05.014).

⁸ See Keyes Rpt. at 37–38 & nn.112, 123, 180 (citing McCabe SE, Schulenberg J, McCabe V V, Veliz PT. Medical use and misuse of prescription opioids in US 12th-grade youth: School-level correlates. *Pediatrics*. 2020;146(4). doi:10.1542/peds.2020-0387; Cano M, Huang Y. Overdose deaths involving psychostimulants with abuse potential, excluding cocaine: State-level differences and the role of opioids. *Drug Alcohol Depend*. Published online October 2020:108384. doi:10.1016/j.drugalcdep.2020.108384; Gaines TL, Wagner KD, Mittal ML, *et al*. Transitioning from pharmaceutical opioids: A discrete-time survival analysis of heroin initiation in suburban/exurban communities. *Drug Alcohol Depend*. 2020;213:108084. doi:10.1016/j.drugalcdep.2020.108084).

⁹ See Keyes Rpt. at 28, 37–38 (reviewing McCabe’s findings that prescription opioid use leads to increased use of heroin whether the prescription opioid use is medical, non-medical, medical followed by non-medical, or non-medical followed by medical).

The Pharmacy Defendants also contend Dr. Keyes' conclusion that a causal relationship exists between prescription opioid and heroin use does not support her inference that prescription opioid use is also responsible for the increase in fentanyl and other synthetic opioid harms. Dr. Keyes' report states:

Available evidence indicates that fentanyl and other high-potency opioids have been adulterating the supply of both heroin and illicitly manufactured prescription opioids. Given the evidence that prescription opioid use is causally related to heroin use, prescription opioid use is also responsible for the increase in fentanyl and other synthetic opioid harms. Indeed, individuals who use prescription opioids who both obtain illicitly manufactured prescription opioids as well as heroin will be potentially exposed to fentanyl, increasing the risk of overdose and death. In terms of the magnitude and scope of the relationship, given that available estimates indicate that approximately 70–80% of individuals who use heroin begin their opioid-using trajectories with prescription opioids, I estimate that approximately 70–80% of fentanyl-involved opioid deaths are attributable to prescription opioid use.

Keyes Rpt. at 39. Given the evidence identified by Dr. Keyes, which indicates an increasing amount of potent, high-risk fentanyl-laced heroin use, Keyes Rpt. at 30–31, 39, it is reasonable to infer a consequential increase in overdose and deaths. The Court finds the reasoning and evidence supporting Dr. Keyes' conclusion correlating prescription opioid and heroin use is a sufficient basis on which to infer the use of heroin adulterated by illicit synthetic opioids increased overdoses and the death toll. *See Globetti v. Sandoz Pharms., Corp.*, 111 F. Supp. 2d 1174, 1176 (N.D. Ala. 2000) (“If scientific methodologies can validate certain facts, scientifically reasonable inferences drawn from those facts are admissible.”); *see also Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 156 (1999) (“[N]o one denies that an expert might draw a conclusion from a set of observations based on extensive and specialized experience.”).¹⁰

¹⁰ *See also Daubert* at 509 U.S. at 589–90 (“The subject of an expert's testimony must be ‘scientific ... knowledge.’ The adjective ‘scientific’ implies a grounding in the methods and procedures of science. Similarly, the word ‘knowledge’ connotes more than subjective belief or unsupported speculation. The term ‘applies to any body of known facts or to any body of ideas inferred from such facts or accepted as truths on good grounds.’”); *Perez v. Texas*, 2014

Jury Confusion and Unfair Prejudice

The Pharmacy Defendants’ final argument posits testimony by Dr. Keyes will mislead jurors to understand her causation opinions as “merely tell[ing] the jury what result to reach” and thereby prejudice Pharmacy Defendants. Motion 16–18. They urge the Court to either exclude testimony attributing to them any responsibility for synthetic opioid-related harms, or provide limiting instructions to the jurors in order to avoid a risk they would understand Dr. Keyes has concluded Defendants were the *legal* cause of the alleged public nuisance. Motion at 17 (citing *Woods v. Lecureux*, 110 F.3d 1215, 1219–20 (6th Cir. 1997) (“ultimate issue” and testimony offering “nothing more than a legal conclusion” is properly excluded). Plaintiffs counter that Dr. Keyes’ opinion regarding the correlation between increased prescription opioid use and increased heroin and fentanyl harms addresses “*factual, not legal, causation.*” Response at 18 (emphasis in original).

Pharmacy Defendants state, “throughout [Dr. Keyes’] report, she draws a causal relationship between various things, like prescription opioids and heroin,” claiming prescription opioids are “responsible” for harms from illicit synthetic opioids, and 70%–80% of fentanyl-related deaths are “attributable” to prescription opioids. Motion at 16. If presented to the jury, Defendants aver, the wording of such testimony would result in a false impression that Dr. Keyes concludes “Defendants were the *legal* cause of a public nuisance.” *Id.* at 17. In that regard, Defendants contend, and Plaintiffs deny, a distinction between but-for and proximate causation is blurred. The disagreement, however, does not warrant precautionary limiting instructions. The

WL 12480146, at *3 (W.D. Tex. July 9, 2014) (expert testimony “necessarily includes any inferences or deductions that the expert may draw from the information he has reviewed and analyzed”).

parties will have the opportunity throughout the trial to explain cause and effect to the jurors. The Court will then provide instructions to the jury to guide their determination of legal responsibility.

Pharmacy Defendants' plea for exclusion of Dr. Keyes' causation opinions is not well-taken. The CDC describes epidemiology as "*a method of causal reasoning* based on developing and testing hypotheses grounded in such scientific fields as biology, behavioral sciences, physics, and ergonomics to explain health-related behaviors, states, and events." Principles of Epidemiology in Public Health Practice, 3d Ed.¹¹ (emphasis added). To preclude an epidemiology expert from testifying to evidence of causal relationships would in large part close the door entirely to the science of epidemiology. It would also go beyond the Court's gatekeeping role under *Daubert*, which instructs that parties should be allowed to rely upon "the capabilities of the jury and of the adversary system general' rather than 'wholesale exclusion' of fairly supported, relevant testimony." *In re Welding Fume Prod. Liab. Litig.*, 2010 WL 7699456, at *23 (N.D. Ohio June 4, 2010) (quoting *Daubert*, 509 U.S. at 596). Where "an expert's scientific testimony rests upon 'good grounds, based on what is known,' *Daubert*, 509 U.S. at 590, it should be tested by the adversary process." *Ruiz-Troche v. Pepsi Cola of Puerto Rico Bottling Co.*, 161 F.3d 77, 85 (1st Cir. 1998); *Burgett v. Troy-Bilt LLC*, 579 F. App'x 372, 376 (6th Cir. 2014) ("the trial court's role as a gatekeeper is not intended to serve as a replacement for the adversary system.' Fed. R. Evid. 702 advisory comm. note, 2000 amend. (quotation marks omitted)").

Accordingly, the Court declines to preclude Dr. Keyes from testifying to evidence and reasoning supporting her opinion that a causal relationship exists between prescription opioid use and harms deriving from synthetic opioid use. *See Ruiz-Troche*, 161 F3d at 85 (otherwise admissible testimony should not be excluded "for fear that [a jury] will not grasp its complexities

¹¹ Available at <https://www.cdc.gov/csels/dsepd/ss1978/lesson1/section1.html>.

or satisfactorily weigh its inadequacies.”). Defendants will have the opportunity to test and refute Dr. Keyes’ opinions through cross-examination and presentation of countervailing evidence.

Conclusion

Accordingly, the Pharmacy Defendants’ motion to exclude certain opinions and testimony of Dr. Katherine Keyes. (Doc. #: 3854) is **DENIED**.

IT IS SO ORDERED.

/s/ Dan Aaron Polster September 13, 2021
DAN AARON POLSTER
UNITED STATES DISTRICT JUDGE